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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,377	04/26/2001	C. Frank Bennett	RTS-0235	1027

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EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/843,377	Applicant(s) BENNETT ET AL.	
	Examiner J. Eric Angell	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 8/1/02 (Paper No. 5). The amendment has been entered and the response to the restriction requirement acknowledged. Claims 1, 2 and 3-20 are pending in the application.

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1, 2 and 2-14) in Paper No. 5 (filed 8/1/02 is acknowledged. The traversal is on the ground(s) that the groups are not patentably distinct because both groups encompass a compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding human Interferon gamma receptor 2 (SEQ ID NO: 3) and a serious search burden does not exist. This is not found persuasive because, as mentioned in the previous Office Action Group I is drawn to a molecule, while Group II is drawn to a method of using the molecule. Therefore, although both Groups encompass the molecule (a compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding human Interferon gamma receptor 2), the molecule can be used in a materially different process of using, namely as a probe in a hybridization assay or as a template for a PCR reaction. Therefore, the restriction is proper and in accordance with MPEP 806.05(h).

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5.

3. Claims 1, 2, and 4-14 are examined herein.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites the phrase, "a compound... which specifically hybridizes with at least an 8 nucleobase portion of an active site on a nucleic acid encoding Interferon gamma receptor 2." (Emphasis added) This phrase renders the claim indefinite because the term "active site" is unclear because the term is not defined in the specification. Therefore it is not clear what constitutes an "active site" and what is not an "active site" of the Interferon gamma receptor 2 gene.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 2, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Soh et al. (Cell 76:793-802; 1994).

The claims are drawn to a compound 8 to 50 nucleobases in length targeted to a nucleic acid molecule encoding human Interferon gamma receptor 2 (SEQ ID NO: 3), wherein said compound specifically hybridizes with and inhibits expression of human Interferon gamma receptor 2 (SEQ ID NO: 3).

Soh teaches a probe that is 20 nucleobases in length that was radiolabelled and used to screen a phage library wherein a clone comprising the sequence of SEQ ID NO: 3 (i.e. human Interferon gamma receptor 2) was isolated (see page 794, last paragraph and page 795, first paragraph and Figure 4). It is noted that Soh referred to the isolated clone as human Interferon gamma accessory factor 1 (Hu-IFN-γ AF-1, hereafter AF-1), however, the sequence of AF-1 is 100% identical to the sequence of SEQ ID NO: 3 (see attached sequence alignment). Therefore AF-1 is human Interferon gamma receptor 1. Although Soh does not specifically teach that the oligo is an antisense to SEQ ID NO: 3, or that the oligo can be used to inhibit the expression of the target gene, Soh does teach that the probe was used to isolate both strands of the gene, indicating that sense and antisense oligos were used. Also, the probe used to identify the sense strand of the target gene (i.e. the antisense oligo) would inherently inhibit the expression of the target gene (Interferon gamma receptor-2). Furthermore, as the definition of "active site" is vague and undefined by the specification, "active site" is considered to be any part of the gene that is transcribed. The oligo taught by Soh specifically hybridizes with the cDNA clone of AF-1; therefore the oligo specifically hybridizes with an active site of AF-1 (SEQ ID NO: 3). Furthermore, Soh teaches the compound was used in a hybridization assay for screening a cDNA

library (see p. 794, column 2; and p. 799, column 2), thus indicating that the probe was in a composition comprising a pharmaceutical acceptable carrier or diluent. Therefore, Soh teaches an oligo that meets all of the limitation of claims 1, 2, 11, and 12.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 4-10, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soh et al. (Cell 76:793-802; 1994) in view of Monia et al (US Patent 6,043,090; March 28, 2000).

Soh teaches a compound 8 to 50 nucleobases (here 20 nucleobases) in length targeted to a nucleic acid molecule encoding human Interferon gamma receptor 2 (SEQ ID NO: 3), wherein said compound specifically hybridizes with and inhibits expression of human Interferon gamma receptor 2 (SEQ ID NO: 3), as mentioned above.

Soh does not teach that the compound comprises (1) a modified internucleoside linkage, such as phosphorothioate; (2) a modified sugar moiety, such as a 2'-O-methoxyethyl sugar moiety; (3) at least one modified nucleobase, such as 5-methylcytosine; (4) that the molecule is a chimeric oligonucleotide; or (5) that the compound is in a composition comprising a colloidal dispersion system.

Monia teaches an antisense compound and composition that specifically hybridizes to and modulates the expression Akt-2. It is recognized that Akt-2 is not related to human Interferon gamma receptor 2 (SEQ ID NO: 3); however, Monia teaches modifications to the antisense molecule which would be obvious to incorporate into other antisense oligonucleotides. Specifically, Monia teaches (1) modifying the backbone of the oligonucleotide (i.e. the internucleotide linkage) to include phosphorothioate (see column5 lines 55-67); (2) modifying the oligonucleotide to contain one or more substituted sugar moieties such as 2'-O-methoxyethyl (2'-MOE) (see column 7, lines 11-36); (3) modifying the oligonucleotide to contain one or more modified nucleobases, such as 5-methylcytosine (5-me-C) (see column 7, lines 56-67); (4) that the oligonucleotide can be a chimeric antisense molecule containing two distinct regions, such as a one region modified to increase resistance to nuclease degradation, increased cellular uptake, and/or increased binding affinity and another region which may be a substrate for a enzyme (such as RNase H) which results in a greatly enhanced efficacy of inhibition of target gene

expression (see column 9, lines 20-45); and (5) that the antisense composition can comprise a hydrophilic colloids (such as polysaccharides or cellulose derivatives) (i.e. a colloidal dispersion system), which are useful in stabilizing the composition (see column 14, lines 35-55).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Soh and Monia to create an antisense oligonucleotide 8 to 50 nucleobases in length that is targeted to SEQ ID NO: 3 (hIFN-γR2) that inhibits the expression of hIFN-γR2 and comprises modifications such as phosphorothioate linkages, 2'-O-methoxyetyhl sugar moieties, 5-methylcytosine, is a chimeric molecule and is in a composition comprising a colloidal dispersion system, with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Monia, who teaches, "such modified or substituted oligonucleotides [i.e. those mentioned above] are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases." (See column 5, lines 20-28). Monia also teaches that, "colloidal solutions stabilize emulsions" (see column 14, lines 45-55).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
October 1, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER